Washington State Department of Health

Prion Diseases
Information for Medical Providers

Introduction

Prion diseases, also known as transmissible spongiform encephalopathies (TSEs), are rare, fatal neurodegenerative diseases of animals and humans. The term prion is derived from the phrase 'proteinaceous infectious particles'. Prion diseases are the result of a specific normal cellular protein folding into an abnormal, pathologic form. This conformational change results in spongiform encephalopathy in cerebral and/or cerebellar cortex, and/or subcortical grey matter.

Sporadic Creutzfeldt-Jakob Disease (sCJD) is the most common human prion disease, accounting for >85% of cases. The overall rate of sporadic CJD worldwide, including in Washington State, is less than 2 persons per million population per year although in persons over 50 years of age, the annual rate is approximately 3.4 cases per million.

To improve knowledge about human prion diseases, Washington's local and state public health departments, in collaboration with the Centers for Disease Control and Prevention (CDC) and the National Prion Disease Pathology Surveillance Center (NPDPSC), are working to increase 1) the recognition and reporting of suspected human prion disease by healthcare providers, and 2) the proportion of prion disease cases that are confirmed through autopsy and tissue examination.

Clinical Features of Human Prion Diseasse

Sporadic CJD is characterized by progressive dementia combined with neurologic manifestations such as myoclonus, visual deficits, cerebellar signs (poor coordination and ataxia), akinetic mutism and pyramidal/extrapyramidal signs. This is a group of distinct diseases and other forms of CJD have different clinical features.

Diagnostic Testing for Prion Diseases

Confirmatory testing for prion disease requires laboratory examination of brain tissue. This is usually done on tissue collected at autopsy. Antemortem indicators are not confirmatory.

Postmortem Testing:

- Brain Autopsy: In suspected cases of prion disease, we strongly recommend that physicians promote the value of autopsy with the patient's family. Arrangements for autopsy and laboratory testing can be made through the National Prion Disease Pathology Surveillance Center (NPDPSC; contact information below). This national reference center provides state-of-the-art prion disease diagnostics, including histopathology, immunohistochemistry, Western blot, and genetic analysis to confirm and determine the type of prion disease. These services are offered free of charge.

Antemortem Indicators:

- Cerebrospinal fluid (CSF) and Protein 14-3-3: CSF findings are generally unremarkable, although mild protein elevation is not uncommon. Testing CSF for the protein marker 14-3-3 may be helpful in patients exhibiting rapidly progressive dementia, however the 14-3-3 marker is not specific or diagnostic for sCJD, and sensitivity decreases as the illness progresses. The test is used when the diagnosis of sCJD is strongly suspected. The National Prion Disease Pathology Surveillance Center (NPDPSC; contact information below) performs 14-3-3 immunoassays free of charge.
- Electroencephalogram (EEG): Obtaining serial EEGs in suspected cases of sCJD is important. In early sCJD, the EEG may be normal or may show non-specific slowing. As disease progresses, biphasic or triphasic synchronous complexes on a slow background evolving into periodic sharp wave complexes occurring at about 1 per second develop. Periodic sharp waves are present at some stage of sCJD in up to 90% of patients and their absence should call into question a diagnosis of sCJD. In contrast, these EEG findings are usually absent in cases of variant CJD.

- Magnetic Resonance Imaging (MRI): Frequently, hyperintense signal in the basal ganglia, thalamus, and cortex which is non-enhancing may be seen on T2- and FLAIR- weighted sequences in cases of sCJD. Diffusion-weighted imaging (DWI) is particularly sensitive, and will often show signal abnormality at the cortical gray-white junction ("cortical ribboning"). While these findings are not specific for CJD, they are helpful in the diagnosis of a clinically compatible case. Suspicion of any form of CJD should be relayed to the interpreting radiologist.

Arranging Autopsy and Post Mortem Testing

Brain autopsy arrangements can be made through the NPDPSC and when local facilities are unavailable, autopsies are usually conducted at Harborview Medical Center in Seattle. All expenses including transport of the body to Harborview, collection of brain tissue, return of the body, shipping, and laboratory testing of brain tissue are covered by the NPDPSC (contact information below). Patients or families interested in autopsy should complete the autopsy consent form found at: http://www.cjdsurveillance.com/pdf/consent-autopsy.pdf.

Reporting a Suspect Case of Prion Disease to a Public Health agency in Washington

Prion diseases in humans are notifiable in Washington as 'Rare diseases of public health significance' (Washington Administrative Code 246-100 and 246-101). All suspected and confirmed cases should be reported to your local health jurisdiction.

Infection Control Considerations

- Prions are resistant to routine disinfectants and methods of sterilization used in medical facilities.
- **Neurosurgical procedures:** Equipment that has been in contact with nervous tissue of a person with a suspected prion disease requires special decontamination procedures. If a patient with suspected or confirmed prion disease requires a neurosurgical or invasive procedure, contact the facility's infection control division to develop and implement appropriate infection control measures.
- **Performing autopsy**: World Health Organization (WHO) Infection Control Guidelines for Transmissible Spongiform Encephalopathies should be followed during autopsy of a patient with suspected or confirmed human prion disease. These can be found at: http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf
- **Tissue/Organ Donation**: Tissues and organs from patients confirmed, suspected, or at risk for prion disease should not be donated for transplantation or teaching purposes.

Additional information about infection control measures related to CJD is available from the Centers for Disease Control and Prevention (http://www.cdc.gov/ncidod/dvrd/cjd/infection_control_cjd.htm) and WHO (http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf).

Obtaining Clinical History to Determine Potential Risk Factors

Human prion disease has occasionally been iatrogenically acquired from human-derived pituitary hormones, dura mater grafts, corneal grafts, and contaminated neurosurgical equipment. Therefore, it is important to obtain a complete history for these exposures on every patient with suspected prion disease. Suspected cases of iatrogenically-acquired prion disease should be reported to your local public health jurisdiction.

Resource for Patients' Families

The CJD Foundation operates a national toll-free line at (800) 659-1991 and a Web site: http://www.cjdfoundation.org/

Contact Information

- Local health departments: http://www.doh.wa.gov/LHJMap/LHJMap.htm
- Washington State Department of Health, Communicable Disease Epidemiology Section: (877) 539-4344 or http://www.doh.wa.gov/EHSPHL/Epidemiology/CD/default.htm
- National Prion Disease Pathology Surveillance Center (NPDPSC), Division of Neuropathology, Case Western Reserve University: (216) 368-0587 or http://www.cjdsurveillance.com